510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
k040452

B. Purpose of Submission:
New device

C. Analyte:
B2-Glycoprotein I Antibodies Screen

D. Type of Test:
Qualitative ELISA

E. Applicant:
Pharmacia Deutschland GmbH/Sweden Diagnostics (Germany) GmbH

F. Proprietary and Established Names:
Varelisa B2-Glycoprotein I Antibodies Screen Kit

G. Regulatory Information:

1. Regulation section:
   21 CFR 866.5660, Multiple Autoantibodies Immunological Test System
2. Classification:
   Class II
3. Product Code:
   MSV, System, Test, Antibodies β2-Glycoprotein I (β2-GPI)
4. Panel:
   Immunology (82)

H. Intended Use:

1. Intended use(s):
   The Varelisa B2-Glycoprotein I Antibodies Screen Kit is designed for the qualitative determination of β2-glycoprotein I antibodies in serum or plasma.
2. Indication(s) for use:
   The presence of B2-glycoprotein I antibodies can be used in conjunction with clinical findings and other laboratory tests to aid in the diagnosis of thrombotic disorders related to the primary Antiphospholipid Syndrome or occurring secondary to systemic lupus erythematosis (SLE) or other autoimmune diseases.
3. Special condition for use statement(s):
   Prescription use only.
4. Special instrument Requirements:
   None.

I. Device Description:

The Varelisa B2-Glycoprotein I Antibodies Screen kit consists of an ELISA strip wells (12 strips X 8 wells) coated with purified human β2-glycoprotein I antigen. It also contains ancillary reagents such as calibrators, negative controls, wash buffer, sample diluent, antibody-chromogen conjugate, enzyme substrate, stop solution for enzyme reaction, and a frame to hold ELISA strip wells. Also included are a package insert and a control certificate.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   INOVA QUANTA Lite B2 GPI Antibody Screen
2. Predicate K number(s):
   k980230
3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Intended Use	Qualitative determination of B2-glycoprotein I antibodies in serum or plasma for use in conjunction with clinical findings and other laboratory tests to aid in the diagnosis of thrombotic disorders related to primary Antiphospholipid Syndrome or occurring secondary to systemic lupus erythematosis (SLE) or other autoimmune diseases.	Qualitative detection of B2-GPI antibodies in serum for use in conjunction with clinical findings and other laboratory tests to aid in the diagnosis of certain autoimmune disease thrombotic disorders, such as those secondary to systemic lupus erythematosis (SLE) or other lupus-like thrombotic diseases.
Antigen	Human affinity-purified β2-glycoprotein I	β2-glycoprotein I, unknown source
Conjugate	Anti-human IgG, IgA, IgM Antibody Conjugate, Horseradish peroxidase	Same
Assay Principle	Indirect noncompetitive enzyme immunoassay	Same
Sample dilution	1:101	Same
Differences		
Item	**Device**	**Predicate**
Specimen	Serum and plasma	Serum
Assay evaluation	Ratio < 1.0 = negative Ratio 1.0-1.4 = equivocal Ratio > 1.4 = positive	Ratio < 1.0 = negative Ratio ≥ 1.0 = positive

K. Standard/Guidance Document Referenced (if applicable):
None

L. Test Principle:
The Varelisa B2-Glycoprotein I Antibodies EIA Kit is an indirect noncompetitive enzyme immunoassay. The wells of the microplate are coated with human purified β2-glycoprotein I antigen. Antibodies specific for β2-glycoprotein I present in the applied patient sample bind to the antigen and are detected by an enzyme labeled secondary antibody complex, which leads to the formation of an enzyme labeled conjugate-antibody-antigen complex. The enzyme labeled antigen-antibody complex converts the added substrate to form a colored solution. The rate of color formation from the chromogen (substrate) is a function of the amount of conjugate complexed with the bound antibody and thus is proportional to the initial concentration of the respective antibodies in the patient sample. The presence of antibodies is calculated by reference of the sample OD to the cut-off OD, and is reported as a ratio of OD sample/OD cut-off.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:
Five serum samples (low, medium, high, equivocal, negative) were selected from a serum bank. The samples were diluted 1:101 and measured in 5 runs, with 4 replicates per run. Standards and controls were analyzed in triplicate. Specified target values were: variance "within" <12%; "between" <10%; "total" < 15%. The specifications were met for each sample, with the following variances:

Sample ID		**Run 1**	**Run 2**	**Run 3**	**Run 4**	**Run 5**	**Mean (U/mL)**	**Variance**		
								Within	Between	total
ZSB 7170	Mean (u/mL)	1.8	2.0	1.9	1.9	1.9	1.9	2.60	3.49	4.35
	CV%	2.82	2.96	2.67	0.0	3.12				
ZSB 7262	Mean (u/mL)	2.7	3.0	2.7	2.9	2.8	2.8	2.12	4.50	4.97
	CV%	0.0	1.68	1.83	3.51	1.8				
ZSB 8300	Mean (u/mL)	3.0	3.2	3.1	3.2	3.1	3.1	2.04	2.48	3.21
	CV%	2.72	2.55	1.89	1.83	0.0				
negative	Mean (u/mL)	0.7	0.6	0.6	0.7	0.7	0.7	11.9	4.9	12.9
	CV%	16.5	8.0	8.7	7.4	14.2				
equiv.	Mean (u/mL)	1.1	1.1	1.0	0.7	1.1	1.1	4.9	4.1	6.4
	CV%	8.5	4.7	0.0	0.0	4.4				

b. Linearity/assay reportable range:
Not done.

c. *Traceability (controls, calibrators, or method):*
Not traceable to external sources. The consistency of the calibration material is given by a testing procedure comprising several internal target values that must be met. Each new production of calibration material is adapted to the corresponding master calibration material.

d. *Detection limit:*
Sample Buffer was diluted according to Directions for Use and measured 88 times on one plate. The Calibrator and the negative control were analyzed in four replicates. Analytical sensitivity was to verify that the background of the assay in less than 30% of the OD of the cut-off.

The sample buffer mean +3SD was 0.080 OD. The calibrator mean OD was 1.93, and negative control mean OD was 0.067. The factor was 0.35 and cut-off OD was 0.694. It was verified that the mean +3SD of the OD of the sample buffer was lower than 30% of the calculated OD of the cut-off.

e. *Analytical specificity:*
Interference was tested against potentially interfering substances found in blood: bilirubin, hemoglobin, chyle, and rheumatoid factor. Three samples from a serum bank were diluted 1:101 and spiked with different super-normal amounts of interferent. Spiked samples were analyzed in triplicate. Acceptance criteria were that spiked samples should show no more than 20% variation from unspiked sample.

Additives (final sample concentration)	**I**	**II**	**III**	**IV**	**V**
Bilirubin F (mg/dL)	0.0	4.8	9.5	14.3	19.0
Bilirubin C (mg/dL)	0.0	5.5	11.0	16.5	22.0
Chyle (Units)	0.0	357.5	715.0	1072.5	1430.0
Hemoglobin (mg/dL)	0.0	122.5	245.0	367.5	490.0
RF (IU/mL)	0.0	98.0	294.0	490.0	-

All samples met acceptance criteria and showed no significant influence on the test results. Additional interference tests on negative and equivocal sera with the same interferents demonstrated a negligible effect of the interferents on the equivocal and negative samples. The negative samples, however, remained negative, so the interference was judged to be not important.

f. *Assay cut-off:*

Qualitative cut-points were determined by measuring 432 samples from apparently healthy Caucasian donors, equally distributed by sex and age. Diluted samples, standards, and controls were analyzed in duplicate. Specifications called for the 95th percentile to be smaller than or equal to the lower limit of the equivocal range. The following values were selected for negative, equivocal, and positive:

Ratio < 1.0 = negative
Ratio 1.0-1.4 = equivocal
Ratio > 1.4 = positive

The specifications were fulfilled and no difference was detected between sexes or ages.

2. Comparison studies:
   a. *Method comparison with predicate device:*
   The following samples were used in comparing the new device with 40 samples from a serum bank at Pharmacia, representing SLE, lupus-like, unknown clinical diagnosis, thrombosis, arthritis, malaria, thalassemia, and healthy individuals. The results were compared in a 6 field analysis. 37 of 40 sera agreed qualitatively (pos/neg) for overall agreement of 92.5%. Two sera were equivocal by the Varelisa assay and either positive (1) or negative (1) by the qualitative predicate. One serum was negative by Varelisa and positive by the predicate.

Varelisa Abs Screen Lot SJ20	n = 40	**INOVA QUANTA Lite Lot 170329**	
		Positive	Negative
	positive	20	0
	equivocal	1	1
	negative	1	17

   b. *Matrix comparison:*
   Twenty blood donor samples in the positive and negative range of the assay were tested in serum, citrate plasma, heparin plasma, and EDTA plasma, in the negative range of the assay. No significant differences were noted for any of the matrices.

3. Clinical studies:
   a. *Clinical sensitivity:*
   Not applicable
   b. *Clinical specificity:*
   Not applicable
   c. *Other clinical supportive data (when a and b are not applicable):*
   Not applicable

4. Clinical cut-off:
   Not applicable
5. Expected values/Reference range:
   Expected value for normal healthy individuals is negative, or ratio <1.0. In a study of 432 healthy Caucasians, the following values were obtained:

N:	432
Mean:	0.54
Mean +2SD	1.24
Median:	0.5
95th percentile	1.0

N. Conclusion:

The submitted information in this premarket notification is complete, and supports a substantial equivalence decision.